NIH POLICY MANUAL

6380-1 - CONTRACTS INVOLVING HUMAN SUBJECTS
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A. Purpose and Applicability:

This issuance states the NIH policies and procedures for the protection of human subjects involved in all projects conducted under NIH research and development (R&D) contracts. (The NIH policy for activities supported by grants is NIH Manual Issuance 4107.) The issuance applies to all research and development contracts involving human subjects except those that are exempt either by Secretarial waiver, as provided by HHS Regulations 45 CFR 46, Section 46.101(e), or that are exempt by section 46.101(b) which reads as follows:

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), if information taken from these sources is recorded in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

3. Research involving survey or interview procedures, except where all of the following conditions exist: (i) Responses are recorded in such a manner that the human subjects can be identified, directly or through identifiers linked to the subjects, (ii) the subject's responses, if they became known outside the research, could reasonably place the subject at risk of criminal or civil liability or be damaging to the subject's financial standing or employability, and (iii) the research deals with sensitive aspects of the subject's own behavior, such as illegal conduct, drug use, sexual behavior, or use of alcohol. All research involving survey or interview procedures is exempt, without exception, when the respondents are elected or appointed public officials or candidates for public office.

4. Research involving the observation (including observation by participants) of public behavior, except where all of the following conditions exist: (i) Observations are recorded in such manner that the human subjects can be identified, directly or through identifiers linked to the subjects, (ii) the

observations recorded about the individual, if they became known outside the research, could reasonably place the subject at risk of criminal or civil liability or be damaging to the subject's financial standing or employability, and (iii) the research deals with sensitive aspects of the subject's own behavior such as illegal conduct, drug use, sexual behavior, or use of alcohol.

5. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

B. Background and References:

1. NIH, PHS and HHS policies for the protection of human subjects have been evolving since 1966. Recent significant changes in the basic HHS regulations (Subpart A of 45 CFR 46) were published January 26, 1981 guided by recommendations of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. In parallel with HHS regulation revisions, the Food and Drug Administration has also published amendments to its regulations regarding the involvement of human subjects in drug testing and clinical trials and for the introduction of new medical devices. These recent revisions require adaptation for NIH policy and procedural compliance.

2. The policies and procedures stated in this chapter implement and supplement:

   a. Public Health Service Act, Title IV, Section 474 (P.L. 93-348, Section 214), Institutional Review Boards; Ethics Guidance Program.

   b. Code of Federal Regulations, Title 21, Subchapters D (Drugs for Human Use), F (Biologics), and H (Medical Devices)

   c. Code of Federal Regulations, Title 41, Subpart 3-4.55 and Section 3-7.5012, Procurements Involving Human Subjects

   d. Code of Federal Regulations, Title 45, Part 46, Protection of Human Research Subjects

   e. HHS Procurement Manual, Subpart 3-4.55, Procurements Involving Human Subjects

   f. HHS Procurement Manual, Subpart 3-7.5012, Procurements Involving Human Subjects

   g. NIH Manual 1730, Forms Management

   h. NIH Manual 2125, Project Clearance Procedure for Public Use Reports

i. NIH Manual 4107, Review of Applications and Award of Grants Involving Human Subjects

j. Policy and Communications Bulletin: The Clinical Center, Group Consideration of Clinical Research Projects 77-1

k. Policy and Communications Bulletin: The Clinical Center, Expedited Review of Clinical Research Projects 81-1

l. NIH Guide for Grants and Contracts, Vol. 8, No. 8, page 29, June 5, 1979, Clinical Trial Activity

m. NIH Guide for Grants and Contracts, Vol. 10, No. 4, page 1, March 6, 1981, Protection of Human Subjects, Temporary Requirement for Form HHS-596

n. Cumulative List of Institutions in General Compliance with HHS Regulations.

C. Responsibilities:

1. The Director and Deputy Director, NIH are responsible for general direction of NIH policies concerning the protection of human subjects.

2. The Associate Director for Extramural Research and Training (ADERT), NIH, determines and establishes NIH policy and procedures for the protection of human subjects in R&D contract projects, and reviews for approval or disapproval all proposed contracts for which records indicate dissenting votes on ethical issues which have not been resolved in reviews, discussions, or negotiations.

3. The Office for Protection from Research Risks (OPRR) discharges the functions under 45 CFR 46 assigned to it by the Office of the Secretary (HHS), PHS, and NIH. The OPRR:

   a. Negotiates and approves assurances with institutions seeking support for research with human subjects.

   b. Assists and advises NIH review groups regarding their responsibilities concerning human subjects.

   c. Assists and advises NIH staff concerning involvement of human subjects in research activities.

   d. Notifies Institutional Review Boards (IRBs) regarding critical comments and evaluations of proposals by peer and other evaluation groups as indicated on summary reports and other documents.

e. Investigates, with the Bureaus, Institutes and Divisions (BIDs), possible instances of noncompliance with Department or NIH policy.

f. Approves all forms, instructions and procedures concerning implementation of this policy.

g. Periodically issues a cumulative list of institutions that have filed assurances with general applicability.

h. Arranges for referral of issues of general ethical concern for appropriate review.

4. BID Directors ensure adherence within their awarding units to established NIH policies. In Bureaus only, those responsibilities assigned to BID Directors may be reassigned to equivalent officials at the Division level.

5. The Director, Clinical Center, reviews and has final approval over planned uses of NIH intramural clinical resources in R&D contract projects involving human subjects, except as covered elsewhere, e.g., see C.2 above.

6. BID and the Division of Contracts and Grants (DCG) Contracting Officers ensure adherence to Health and Human Services Procurement Regulations (HHSPR) Subpart 3-4.55, and other applicable HHS and Federal Regulations in awarding and terminating contracts involving human subjects, and expediting the processing and review of contract proposals.

7. Within BIDs, the Director or Associate Director of BID extramural activities programs (EAP), ensures adequate technical evaluation of projects involving human subjects. In addition, these individuals are responsible (a) for alerting the OPRR and their concerned BID personnel to the needs for negotiating assurances and to possible noncompliance with established assurances, as well as evidence of procedural deficiencies in required reviews by IRBs, and (b) for ensuring appropriate corrective actions.

8. Project Officers for contracts involving human subjects must have appropriate preparation to monitor contractor performance, identify unforeseen hazards, identify deviations from or use of procedures not specified in the original protocols, and report to OPRR any noncompliance with 45 CFR 46.

D. Definitions:

1. Certification The official notification by the institution to HHS that the research project or activity involving human subjects has been reviewed and approved by the IRB in accordance with the approved assurance on file at OPRR. Certification is required when the research is funded by the Department and not otherwise exempt in accordance with 46.101.

2. Cumulative List A list of institutions, with HHS-approved assurances with general applicability, which is published and distributed periodically by the

OPRR.

3. Expedited Review A procedure for review and approval of research covered by 45 CFR 46 in which the IRB Chairman or another experienced reviewer from among IRB members may perform all IRB functions except disapproval of the research activity for research procedures that are (a) no more than minimal risk and (b) on the list published by the Secretary in the Federal Register. Minor changes in previously approved research may also be reviewed by expedited review during the period of project approval.

4. Human Subject A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. (See 46.102(f).)

5. Informed Consent The knowing consent of an individual or the individual's legally authorized representative, under circumstances that allow sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The basic elements of informed consent are:

   a. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;

   b. A description of any reasonably foreseeable risks or discomforts to the subject;

   c. A description of any benefits to the subject or to others which may reasonably be expected from the research;

   d. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

   e. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

   f. For research involving more than minimal risk, an explanation as to whether compensation is available and an explanation as to whether any medical treatment is available if injury occurs and, if so, what they consist of, or where further information may be obtained;

   g. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and

h. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

6. Institution Any public or private entity or agency (including federal, state, and other agencies).

7. Institutional Assurance The documentation, on file with or submitted when requested by OPRR, from an institution seeking PHS support assuring institutional compliance with and implementation of 45 CFR 46 on protection of human subjects.

8. Institutional Review Board (IRB) A board or committee charged with responsibility for review of research activities involving human subjects conducted at or sponsored by the institution. The composition of the IRB and details of its procedures and responsibilities are specified in 46.103(b)(3) and included in the institutional assurances as approved by HHS (OPRR).

9. Minimal Risk The risk of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

E. Policy:

1. Institutional Responsibility Safeguarding the rights and welfare of subjects in activities under NIH R&D contracts is primarily the responsibility of every institution which receives or is accountable to NIH for funds awarded for the conduct of such activity. To ensure that this institutional responsibility is accomplished adequately, policy provides that NIH shall not permit a nonexempt research activity involving human subjects to be undertaken unless the institution has an assurance on file with the Department and has certified to NIH that an IRB has reviewed and approved such activity in accordance with 45 CFR 46.

2. NIH Responsibility NIH will award contracts involving human subjects only to institutions which assume responsibility for the subjects involved. Under no circumstances will NIH allow a contract project to involve human subjects until the institution has provided an acceptable assurance of compliance to OPRR and NIH has received certification of IRB review approval.

3. BID Responsibility The BIDs awarding R&D contracts have responsibility for the determination that all regulatory and policy requirements are met and that the rights and welfare of human subjects have been and will be adequately protected. Evaluation through appropriate review mechanisms, e.g., technical merit or BID staff review, will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the proposed research to the subjects and others, and the importance of the

knowledge to be gained.

F. Solicitation:

1. Project Initiation At the stage of concept review, consideration must be given to the rights and welfare of proposed subjects. Program officials should seek OPRR's and advisory groups' recommendations on potential risks to subjects, protections against risks, risk-benefit relationships, adequacy of informed consent procedures and other such issues concerning proposed projects. Appropriate advisors, knowledgeable on issues relating to human subjects protection, may be consulted to help resolve outstanding issues. All deliberations regarding subjects' rights and welfare shall be documented; the record shall indicate whether the approval of a project concept was unanimous. If there were abstentions and/or dissents, these must be documented.

2. Request for Proposals (RFP) Before solicitation, when contract performance is expected to involve human subjects, the Directors or Associate Directors of EAP or their designees shall review and approve all RFPs to ensure that they include appropriate provisions to protect human subjects. Contracting Officers shall include in Requests for Proposals the notice to offerors specified in HHSPR 3-4.5504(a). RFPs must specify whether offerors' assurances and certifications must be submitted, including requirements for submitting Form HHS-596.

   For each solicitation involving research with human subjects, notification of the applicability of 45 CFR 46 and special considerations, if any, pertaining to human subjects involvement, should be included. The Request for Proposals should clearly indicate that HHS-approved assurances and certifications will be required of each offeror selected for final consideration for an award.

3. Institutional Prerequisites

   a. Declaration and Assurances

   Section 474(a) of the PHS Act and HHS regulations require that each institution applying for funds for research involving human subjects have an approved assurance or submit with each research proposal involving human subjects a declaration that the institution has established an Institutional Review Board and, when requested, will submit to HHS such additional assurances and certifications as may be required for implementation of regulation 45 CFR 46 (see Form HHS-596). Additional assurances with certification will be negotiated by OPRR when requested by a BID. Assurances approved by OPRR for specific projects include certification for the initial year of support.

   b. Form HHS-596 Certification Requirements

   An institution with an acceptable assurance on file with OPRR (i.e., the institution is included on the Cumulative List or has an assurance previously

approved for the specified project) must certify initially before technical merit review of the proposal and annually to the Contracting Officer that the research involving human subjects is in accordance with 45 CFR 46 (see Form HHS-596).

(1) Institutions with assurances on file must submit certifications either (a) within 60 days after the receipt date deadline for which the proposal was submitted; or (b) if no deadline was specified, within 60 days following the actual proposal submission date.

(2) Institutions not having an assurance on file must have submitted assurances with certification for the initial year as in F.3.a., above.

(3) When 46.118 applies, i.e., delayed involvement of human subjects has been previously approved by a BID but not certified by a contractor, the contractor may not proceed before certification is received and the BID's authorization is given.

c. Certification Requirement for Proposed Change in Workscope to Involve Human Subjects

When 46.119 applies, i.e., involvement of human subjects without previous BID approval in an ongoing research project, the Contracting Officer shall request OPRR assurance negotiation, if required. Certification with the proposed change in work-scope from the Contractor must be submitted. Authorization to proceed is the responsibility of the Director or Associate Director of BID extramural activities programs, who shall determine whether BID committee review is required.

d. Additional Certifications

A BID may request additional IRB review and certification for a proposed or ongoing research activity whenever BID personnel are concerned that the rights or welfare of human subjects are not adequately protected or that subjects may be at increased or additional risks not fully considered in previous IRB review. OPRR should be consulted before additional certification is requested.

G. Review of Proposals:

NIH requires BID review of contract proposals in accordance with 45 CFR 46.120.

1. Preliminary Staff Review

a. Contracting Officers are responsible for ensuring that an acceptable Form HHS-596 (exemption, declaration, certification, or timely IRB review pending date) accompanies (1) each proposal responding t an RFP which specifies

research involving human subjects and (2) each unsolicited proposal, suggesting research with human subjects, which the BID accepts. If an HHS-596 has not ben submitted or is not acceptable, the Contracting Officer will send a letter and Form HHS-596 to the official signing for the institution, and a copy of the letter to the principal investigator, indicating what steps must be taken, the due date for an acceptable form, and the consequences of failure to submit the form on time or at all.

b. If an acceptable Form HHS-596 has not been received by the time of technical merit evaluation, the Contracting Officer will notify those offerors that the BID will not consider those proposals beyond the technical merit review stage and will not inform the offerors of their standing until an acceptable HHS-596 is received.

2. Technical Merit Evaluation

a. Review Group Evaluation - Groups that review contract proposals for technical merit should be requested also to assist in evaluating the ethical acceptability of an offeror's procedures involving research with human subjects. The evaluation shall take into account such factors as:

(1) apparent risks to subjects, including not only medical risks but also psychological and social risks;

(2) adequacy of protection against identified risks;

(3) the potential benefits of the proposed research to the subjects and others;

(4) the importance of the knowledge to be gained;

(5) adequacy and appropriateness of the informed consent procedure.

b. Review Recommendations - Although the proposal may be evaluated as either acceptable or unacceptable based on technical merit, with respect to each proposed activity involving human subjects the review group may recommend:

(1) approval of the activity without restrictions;

(2) approval of the activity, but with expressions of concerns, or contingent on limitations, restrictions, or elimination of procedures involving human subjects;

(3) deferral for further evaluation, if feasible; or

(4) disapproval of one or more of the activities, due to inadequate

protection or unacceptable risks.

c. Summary Statements - Executive Secretaries shall document reviews, evaluations, and recommendations with respect to the topics in G.2.a. and b., and in addition shall use "Administrative Notes" to call attention on summary statements to any unresolved problems. Executive Secretaries shall send copies of summary statements having "Administrative Notes" to OPRR as soon as available, whether judged acceptable or unacceptable. OPRR will request a copy of the proposal, if needed. Examples of special notations are:

(1) HUMAN SUBJECTS - POTENTIAL RISKS - Where appropriate, the Executive Secretary should follow the evaluation with a separate paragraph headed "HUMAN SUBJECTS," identifying unacceptable risks or procedures, giving reasons, and stating what procedures, if any, should be modified or entirely deleted, in the opinion of the majority of the members of the technical evaluation group. Any suggested communications to offerors concerning human subjects should also be developed as completely and clearly as possible.

(2) HUMAN SUBJECTS - RESEARCH RESTRICTED - To indicate that the proposed research may require special ethical review in accordance with 45 CFR 46 or may otherwise be restricted or prohibited, e.g. involving human in vitro fertilization, fetuses, pregnant women, or prisoners.

3. Source Selection In evaluating proposals for contract awards, BIDs may take into account, in addition to all other eligibility requirements and program criteria, such factors as whether:

   a. The offeror has previously been subject to a termination or suspension under 45 CFR 46.123 or 45 CFR Part 74;

   b. The offeror or the persons who would direct the scientific and technical aspects of a project, are judged by the BID or NIH to have failed materially to discharge their responsibilities to protect the rights and welfare of subjects in their care, whether or not HHS funds were involved; and

   c. Adequate steps have been taken to eliminate past deficiencies where they have existed.

4. Request for Assurance Negotiation To ensure timely OPRR negotiations of assurances with certifications, for the institutions not on the Cumulative List, the Contracting Officer should request negotiations well in advance of planned awards.

   a. An institution with an approved assurance normally need only certify on Form HHS-596 to the BID Contracting Officer. In exceptional or uncertain

circumstances (see G.2 and G.3 above for examples), OPRR shall be consulted for possible negotiation of additional assurances.

b. The Contracting Officer should anticipate a 3-6 week delay for a response following a request for an assurance from an institution not on the Cumulative List. For a sole source proposal, or for each proposal determined to be in the competitive range, a request for assurance negotiation should be accompanied by a summary statement, Proposal Summary and Data Record (Form NIH-2043), and a duplicate of the signed HHS-596. OPRR may request a copy of the complete proposal if needed.

5. Review Follow-up The Contracting Officer, with concurrence by the Project Officer, should communicate in writing, both to officials signing for offerors and to investigators, information regarding all suggested restrictions, contingencies, or expressions of concern for the involvement of human subjects, whether or not the proposal may lead to award. A copy of all relevant documents should be sent to the Project Officer and OPRR.

H. Additional Considerations:

Further pre-award review and approval depend on additional factors.

1. Extramural Resources Involving Human Subjects

   a. All proposed contracts involving research with human subjects shall be reviewed further by the BID Program Director and the medically qualified Director or Clinical Director of the BID or Division of a Bureau, or other designees. Directors or their designees may require additional reviews by the Clinical Research Subpanel or other suitable committees of their BIDs.

   b. When NIH technical merit evaluation groups or source selection groups have indicated concerns or reservations regarding a proposed contractor's plans for work with human subjects, the BID program staff may, in consultation with OPRR, request a copy of the record of the IRB's review and approval of the project, and a copy of the informed consent form the institution proposes to use.

   (1) The IRB record should state if approval was unanimous or, if there were abstentions or dissenting votes, the number of such votes and the reasons for nonconcurrence.

   (2) The informed consent must include as a minimum the basic elements of information included in 46.116, as outlined in D.5. above, unless the IRB has modified or waived some or all of the elements of informed consent in accordance with 46.116(c) or (d). The IRB must document any such modification or waiver.

   (3) Informed consent must be documented as provided in 46.117. If a

"long form" or "short form" consent document is not to be obtained for each subject under the procedures described in that section, the IRB record must document specifically that such modification is supported by their findings that:

(a) the only record linking the subject and the research would be the consent document and the principal risk would be the potential harm resulting from a breach of confidentiality. Each subject will be asked whether he or she wants documentation linking the subject with the research, and the subject's wishes will govern; or

(b) the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. In many cases it may be appropriate for the Board to require the investigator to provide subjects with a written statement regarding the research.

c. The BID Contracting Officer shall advise offeror institutions of the BID's findings or concerns regarding informed consent documents, and may require, as conditions for award, that those documents contain minimum conditions and actually reflect program requirements. BIDs may not, however, require deletions from those documents which might be contrary to local laws or other standards.

2. Intramural Resources Involving Human Subjects

a. All contracts utilizing intramural resources (e.g. NIH staff or records) shall be reviewed by the Clinical Research Subpanel of the BID or Division of a Bureau, the Institute's Clinical Director, and the Director, Clinical Center. This requirement governs contract projects which are:

(1) funded through intramural BID clinical programs or the Clinical Center portion for the Management Fund; or

(2) conducted by employees of BID intramural clinical programs or the Clinical Center, in connection with their responsibilities or relationships to the Clinical Center, or who intend to identify the Clinical Center in any report of the activity; or

(3) using Clinical Center records and personnel to identify and/or contact clients, patients, or normal volunteers to be subjects.

b. The Director, Clinical Center, shall have the final authority to allow NIH intramural resources to be used in contract research which has been previously reviewed and approved by the BID Clinical Research Subpanel.

3. Office of Director, NIH

   If the records on previous reviews show dissenting votes on ethical issues which have not been reviewed, the BID must submit the proposed contract to the Associate Director for Extramural Research and Training, NIH, for approval or disapproval.

4. Special Reviews

   a. Proposal involving areas of investigation or subjects in categories designated by the Secretary, or Director, NIH, for special ethical review shall be referred for review in accordance with 45 CFR 46.

   b. Forms Management (NIH Manual 1730) and Project Clearance Procedure for Public Use Reports (NIH Manual 2125) outline procedure requirements for questionnaires and other reporting forms.

I. Contract Award:

1. Negotiations

   a. Responsible BID Project Officers must resolve with the offeror all unacceptable risks or related scientific concerns that were identified in the NIH review process. If human subjects issues are not resolved before contract negotiation, the Project Officer should refer the proposal to an appropriate NIH review group for recommendation and advice and inform OPRR.

   b. For each proposal in the competitive range which requires negotiation of an assurance, the BID Contracting Officer should forward to OPRR a request for negotiation of the assurance, attaching a copy of the proposal, summary statement, and any additional documentation.

c. If the contractor proposes toinvolve subjects through cooperating institutions, the Contracting Officer should determine, in consultation with OPRR, whether it is desirable to obtain assurances or certifications from any of these institutions which are not on the Cumulative List.

2. Awards

   a. NIH contract projects may involve human subjects only if the workscopes, initially or by amendment, specifically provide for participation of human subjects. Statements specifically forbidding work with human subjects must be included in the workscopes of all other contracts.

   b. The clause specified in HHSPR 41 CFR 3-7.5012 shall be included in all NIH contracts involving human subjects. In addition, the special conditions of each such contract may specifically restrict certain activities involving human

subjects, such as procedures or certain subject groups, or may require use of specified safeguards. The contract may stipulate minimum requirements to be included in the informed consent document, such as specific risks, discomforts, benefits, and alternative procedures, e.g., other therapeutic measures. The contract may simply list these items or may provide a model consent form, and must make clear that any such list or model constitutes only a minimum which may be expanded by the contractor to identify additional items or to satisfy requirements of applicable state or local laws relating to informed consent. Whenever there is any question, the BID Contracting Officer or program staff should consult with OPRR and possibly the NIH Legal Advisor, OGC.

c. Proposals lacking definite plans for involvement of human subjects (45 CFR 46.118) or those which do not intend to involve human subjects (45 CFR 46.119) need not be reviewed by the Institutional Review Board before an award may be made. Except for research exempted by 46.101(b), no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the Institutional Review Board and certification submitted to and accepted by the Contracting Officer. Changes pursuant to 45 CFR 46.119 must be approved by HHS.

J. Contract Administration:

1. Periodic Review

   The Contracting Officer, with advice from the Project Officer, will ensure that an IRB shall conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. One copy of an acceptable HHS 596 must be submitted with each annual report.

2. Amendments

   Directors of BIDs or Divisions or Bureaus will establish procedures and guidelines by which amendments of contracts involving human subjects will be reviewed. The Directors shall determine if amendments, e.g., concerning procedures or characteristics of subject population groups, warrant referral to review groups such as mentioned in G.2. and H.4. a above.

3. Early Terminations and Conditions

   Early terminations of research funding and evaluations of subsequent applications and proposals are discussed in 45 CFR 46.123.

   Under 45 CFR 46.124 additional conditions may be imposed by the BID before or at the time of an award when those conditions are judged necessary for the protection of human subjects.

4. Records

a. Records to be maintained by institutions are discussed in 45 CFR 46.115.

b. Bids will maintain records on each contract involving human subjects which will include: (1) the contractor's annual certification or a letter indicating that the assurance has been approved by OPRR; (2) copies of summary statements, memoranda, correspondence with investigators, and other documents identifying concerns for the welfare of subjects, whether the final actions are for award or not. Documentation of evaluations made and recommendations given by contractors' advisory groups, including minutes of the contractors' clinical research committees, may be requested by the BID Program or Project Officers through OPRR when additional information is needed, or may be optionally supplied by the contractors.

c. The Contracting Officer, with advise from the Project Officer, must keep OPRR informed on all matters of substantive concern regarding human subjects.

K. Additional Information:

For further information contact: OERT/OD, 496-2241.

L. Additional Copies of NIH Manual Chapters:

For copies of this manual chapter send a memorandum to the Printing and Reproduction Branch (P&RB), DAS, Building 31, Room B3BE07; or call OERT/OD, 496-2241.